Remarks

Claims 1-12 and 15-17 have been canceled without prejudice to the filing of continuing applications. New claims 20-31 have been added. No new matter is added with these claims. Claims 18 and 19 have been amended by adding the term "methoxymorpholino doxorubicin" to reflect the meaning of the acronym "MMDX". No new matter is added with this amendment. A marked-up copy of the amended claims is included herewith.

As claims 1-12 and 15-17 have been canceled, withdrawal of the rejection based on 35 U.S.C. § 112 is respectfully requested.

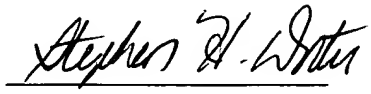
Claims 13, 14, 18 and 19 stand rejected under 35 U.S.C. § 103 as being unpatentable over Kuhl et al. in combination with Miura et al. Specifically, Miura teaches the treatment of liver tumors or hepatocellular carcinomas via hepatic artery administration of doxorubicin and lipiodol to decrease tumor volume or cause remission. Kuhl teaches that MMDX is a doxorubicin analog that has the same tumor specificity as doxorubicin, and also is activated in the liver to a metabolite whose potency is 10 times greater. The Examiner contends that a person skilled in the art would have been motivated to use MMDX to treat solid tumors in the liver via the hepatic artery.

Applicants respectfully disagree with the obviousness rejection for the following reasons. Miura does not teach nor remotely suggest the use of MMDX for the treatment of liver tumor by administering MMDX directly to the liver via intrahepatic route. The fact that MMDX belongs to the family of anthracyclines including doxorubicin, for which activity in hepatic tumors has been disclosed in Miura, can not be considered as predictable of the efficacy of MMDX in the same tumor setting, i.e. solid tumors of the

liver. Kuhl discloses that MMDX is activated in the liver to a metabolite whose potency is 10 times greater, but nothing is taught or suggested about its efficacy in solid tumors such as liver tumors; the potential of MMDX is assessed only in liquid tumor models, i.e. in a panel of 14 different human leukemia and lymphoma cell lines. The prior art simply does not provide a reasonable expectation of success that MMDX could be used to treat solid liver tumors. While MMDX is an analog of doxorubicin, it can not be predicted by those skilled in the art to behave similarly in every tumor model. The compounds are structurally distinct and have distinct and separate status in the art and would thus be expected by those skilled in the art to have different biological properties. With the present invention, Applicants have shown by much experimentation that MMDX chemotherapy through the hepatic artery is effective for patients with liver cancers (see "Activity" section at page 13 of the specification). In view of the above, a person skilled in the art would not be motivated to replace doxorubicin with MMDX combining the above indications of Miura and Kuhl for treating a liver tumor because he/she would not have a reasonable expectation of success for an effective treatment for this tumor type. Withdrawal of the obviousness rejection is respectfully solicited.

Allowance of the claims and passage of the case to issue are respectfully solicited. Should the Examiner believe a discussion of this matter would be helpful, he is invited to telephone the undersigned at (312)-913-0001.

Respectfully submitted,

By: 

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Marked-up Copy of Claims for U.S.S.N. 09/786,998

Claims 18 and 19 have been amended as follows.

18. (Amended) A method of treating a human liver tumor which comprises the intrahepatic administration of a therapeutically effective amount of methoxymorpholino doxorubicin (MMDX) to a patient in need thereof.

19. (Amended) A method for reducing methoxymorpholino doxorubicin systemic exposure of a patient suffering from a liver cancer which comprises the intrahepatic administration of a therapeutically effective amount of methoxymorpholino doxorubicin (MMDX) to said patient.